THE CLAIMS

What Is Claimed Is:

1. A culturing system, comprising:

(a) a medium reservoir containing a growth medium;

(b) a tangential flow growth device connected to the medium reservoir, said tangential flow growth device having a medium flow control means;

(c) a pump system having discharge and inlet ports for pumping the medium from the medium reservoir to the tangential flow growth device;

(d) a sterile barrier tangential flow membrane device connected to the tangential flow growth device;

(e) a means for monitoring medium conditions; and

(f) a means for harvesting cells grown in the tangential flow growth device, said harvest means openably and closably connected to the tangential flow growth device;

2. A culturing system according to claim 1, wherein said cells produce infective viruses and wherein said means for harvesting cells comprises a vessel, and said vessel is connected to a source of chemical capable of inactivating said viruses to render them uninfective.

3. A culturing system according to claim 1, wherein the tangential flow growth device comprises a mass transfer culture system.

4. A culturing system according to claim 3 wherein said

medium flow control means comprises flow ports designated A, B, C, and D, for connecting:

(a) in a first configuration, port A in flow communication with port B, and port C in flow communication with port D; and

(b) in a second configuration, port A in flow communication with port D, and port B in flow communication with port C; and wherein said medium reservoir has inlet and outlet ports; and wherein said mass transfer culture system has an elongated mass transfer chamber having first and second inlets at opposite ends of the chamber and conduits connecting the pump discharge port to said port C, the pump inlet to the reservoir outlet port, the reservoir inlet port to the port A, the chamber first inlet to the port B and the chamber second inlet to the port D.

5. A culturing system according to claim 3, wherein the sterile barrier tangential flow membrane device comprises a stacked plate filter system.

6. A culturing system according to claim 5, wherein said stacked plate filter system comprises:

(a) a support including a circumscribing frame with an array of spaced-apart and substantially parallelly aligned ribs extending between and joined at their opposite ends to said frame, so that the ribs and frame form a series of corresponding substantially parallel filtrate flow channels, and openings in said frame in liquid flow communication with said filtrate flow channels for egress of filtrate from said filtrate flow channels through said frame openings;

(b) a first filter sheet continuously secured along its margins to a first face of said frame; and

(c) a second filter sheet continuously secured along its margins to a second face of said frame;

(d) the first and second filter sheets together with the frame defining an enclosed interior volume comprising said filtrate flow channels separated by said ribs;

(e) whereby filtrate entering said enclosed liquid volume through said first and second filter sheets may flow in said filtrate flow channels and be discharged from said filter element through said frame openings in liquid flow communication with said filtrate flow channels.

7. A culturing system according to claim 5, wherein said stacked plate filter system comprises a stacked plate filter for use with a disposable sheet filter element, said stacked plate filter comprising:

(a) a first generally planar and rectangular filter plate having a substantially flat bottom surface, and a top surface with an unwardly extending wall circumscribingly bounding a flow channel of generally rectangular shape with a liquid inlet port at a medial part of a first side of said flow channel and a liquid outlet port at a medial part of a second side of said flow channel opposite said first side thereof, said liquid inlet port being joined in liquid flow communication with a liquid feed trough extending transversely across said first side of said flow channel, and said liquid outlet port being joined in liquid flow communication with a liquid collection trough extending transversely

across said second side of said flow channel, with a plurality of spaced-apart partitions extending upwardly from the floor of said flow channel between said liquid feed trough and said liquid collection trough, said partitions being of lesser height than said wall circumscribing said flow channel and substantially parallel to each other to define a series of sub-channels extending longitudinally between said liquid feed trough and said liquid collection trough, said liquid feed trough being of progressively decreasing depth from its medial portion, in communication with said liquid inlet port, to its marginal extremities, and said liquid collection trough being of progressively decreasing depth from its medial portion, in communication with said liquid outlet port, to its marginal extremities;

(b) a foraminous support of generally rectangular shape supportively reposable at a first face thereof on said partitions of said first filter plate;

(c) a second filter plate structurally identical to said first plate member, positioned in inverted relationship to said first plate member such that said circumscribingly bounding walls of said first and second filter plates are in abutting contact with one another, with said foraminous support betwen said first and second filter plates and supported by the respective partitions thereof; and

(d) filter sheets on either side of the foraminous support, interposed between the foraminous support and the supporting partitions of the respective first and second filter plates.

8. A culturing system according to claim 5, wherein said

stacked filter plate system comprises a filter plate having a generally planar and rectangular shape with a substantially flat bottom surface, and a top surface with an upwardly extending wall circumscribingly bounding a flow channel of generally rectangular shape, with a liquid inlet port at a medial part of a first side of said flow channel and a liquid outlet port at a medial part of a second side of said flow channel opposite said first side thereof, said liquid inlet port being joined in liquid flow communication with a liquid feed trough extending transversely across said first side of flow channel, and said liquid outlet port being joined in liquid flow communication with a liquid collection trough extending transversely across said second side of said flow channel, with a plurality of spaced-apart partitions extending upwardly from the floor of said flow channel between said liquid feed trough and liquid collection trough, said partitions being of lesser height than said wall circumscribing said flow channel and substantially parallel to one another to define a series of sub-channels extending longitudinally between said liquid feed trough and said liquid collection trough, said liquid feed trough being of progressively decreasing depth from its medial portion, in communication with said liquid inlet port, to its marginal extremities, and said liquid collection trough being of progressively decreasing depth from its medial portion, in communication with said liquid outlet port, to its marginal extremities.

9. A culturing system according to claim 3, wherein the medium flow control means comprises a switchable flow control means for controlling the direction of flow of medium through the mass transfer culture system.

10. A culturing system according to claim 9, wherein the growth medium is capable of growing host cells for viral pathogens and the means for harvesting cells comprises a virus removal, concentration and lysis system.

11. A culturing system according to claim 1, further comprising a culturing system control means for automatically controlling medium flow.

12. A culturing system according to claim 5, further comprising a means for nutrient exchange into and out of the growth medium.

13. A method of growing cell cultures using a closed culturing system to produce a cell product, comprising the steps of:

(a) inoculating a mass transfer culture system having a switchable flow control means with cells capable of producing a desired cell product;

(b) exposing the cells to a flowing cell growth medium;

(c) periodically changing direction of flow of the cell growth medium with the switchable flow control means;

(d) adjusting medium components to optimize cell product production by means of a sterile barrier tangential flow membrane device; and

(e) filtratingly concentrating the cell product by removal of liquid from the medium without removing cell product from the microbial culturing system; and

(f) removing low molecular weight inhibitory substances by membrane dialysis of the flowing cell growth medium.

14. A method according to claim 13, wherein said mass transfer culture system comprises flow ports designated A, B, C, and D, for connecting:

(a) in a first configuration, port A in flow communication with port B, and port C in flow communication with port D; and

(b) in a second configuration, port A in flow communication with port D, and port B in flow communication with port C; and

wherein said mass transfer culturing system comprises a first pump having discharge and inlet ports; an elongated mass transfer chamber having first and second inlets at opposite ends of the chamber; a reservoir having inlet and out ports; and

conduits connecting the pump discharge port to said port C, the pump inlet to the reservoir outlet port, the reservoir inlet port to the port A, the chamber first inlet to the port B and the chamber second inlet to the port D.

15. A method for growing cell cultures to produce a cell product according to claim 13, wherein the cell product comprises a cellular pathogen.

16 A method for growing cell culture to produce a cell product according to claim 15, wherein the cellular pathogen is a virus.

17. A method for growing cell cultures to produce a cell product according to claim 15, further comprising treating of the cell product to destroy pathogenicity after the cell product is filtratingly concentrated.

18. A method according to claim 13, wherein said cell product is HIV virus.

19. A method according to claim 13, wherein said cell product is a virus.